

# Discovering Glioma Inhibitors via Chemical-genetic Screens in *Drosophila* Cancer Models



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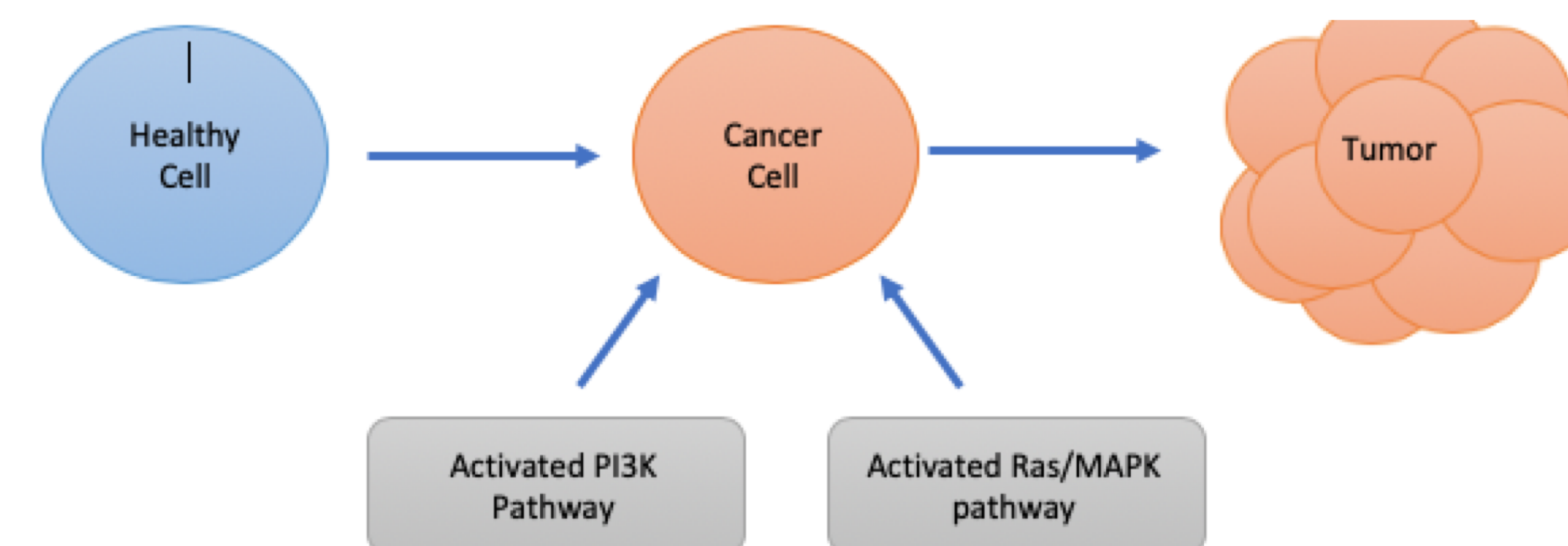
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## Abstract

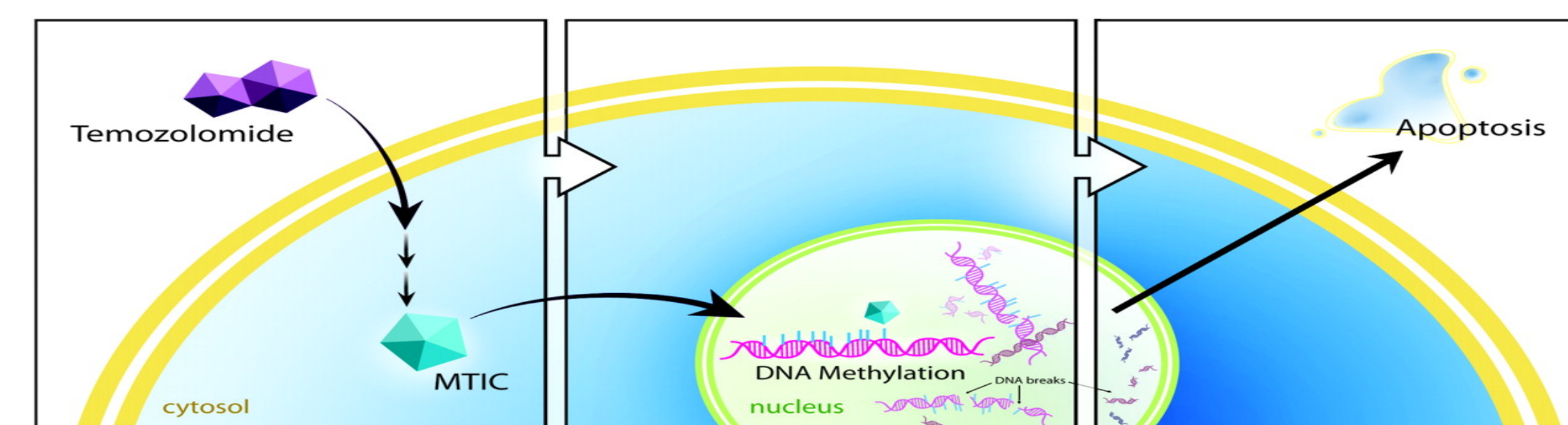
Today, there are over 250 drugs being used to cure over 100 different types of cancer, and one that might prove effective for a certain type of cancer might prove harmful or ineffective for another type. We plan to screen a chemical library of tyrosine kinase inhibitors to test their effects on glioma growth in a GAL4xUAS *Drosophila* glioma model. We first tested Temozolomide to establish proof of principle. Next, we compared this to a group of Tyrosine Kinase inhibitors. We found both enhancers (positive regulators) that increase glioma growth, and repressors (negative regulators) that suppress the growth of the tumor through this screen. However, none of the drugs caused a significant suppression without unwanted lethality suggesting that a better approach is to use low doses of different drugs in combination rather than increase the dose of a single drug- which is likely responsible for lethal effects observed.

## Glioma Progression



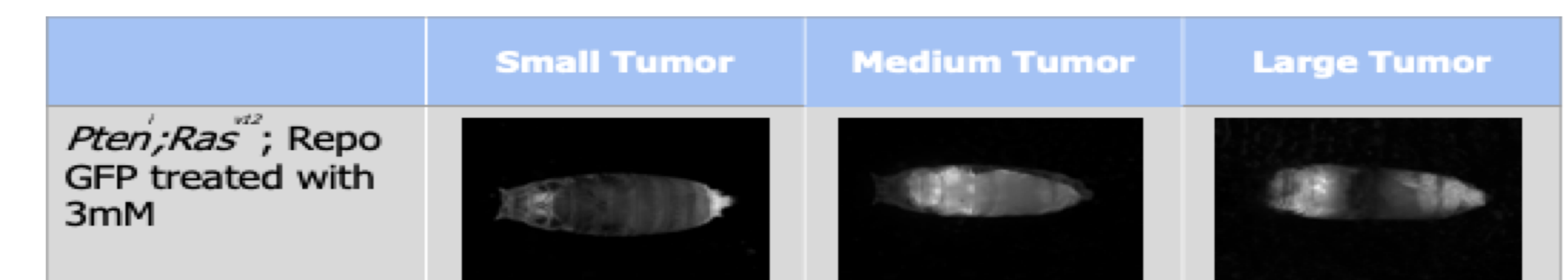
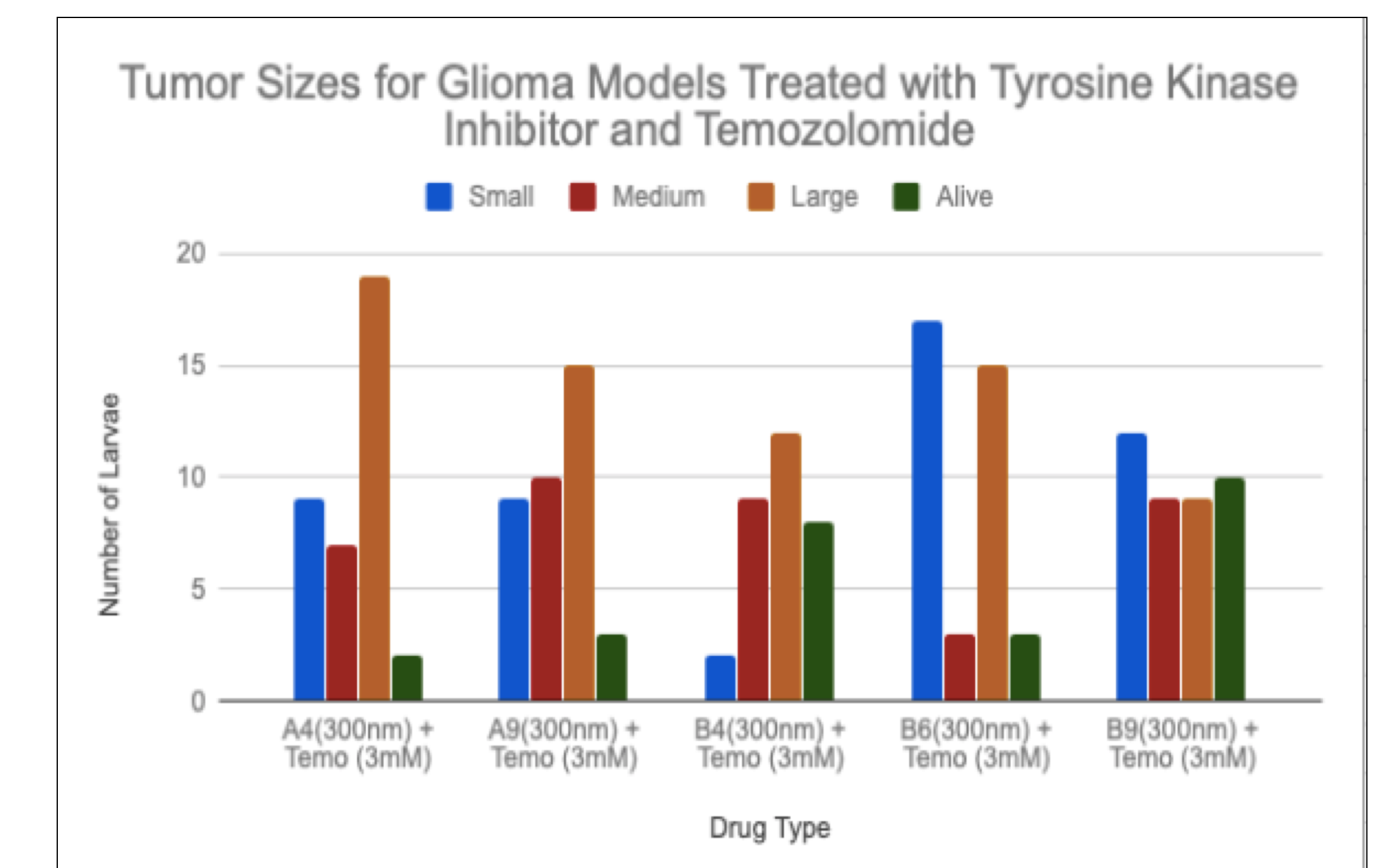
## How Temozolomide Impacts

Temozolomide is a DNA alkylating agent that is being used in glioma treatment due to it leading to apoptosis



## Results

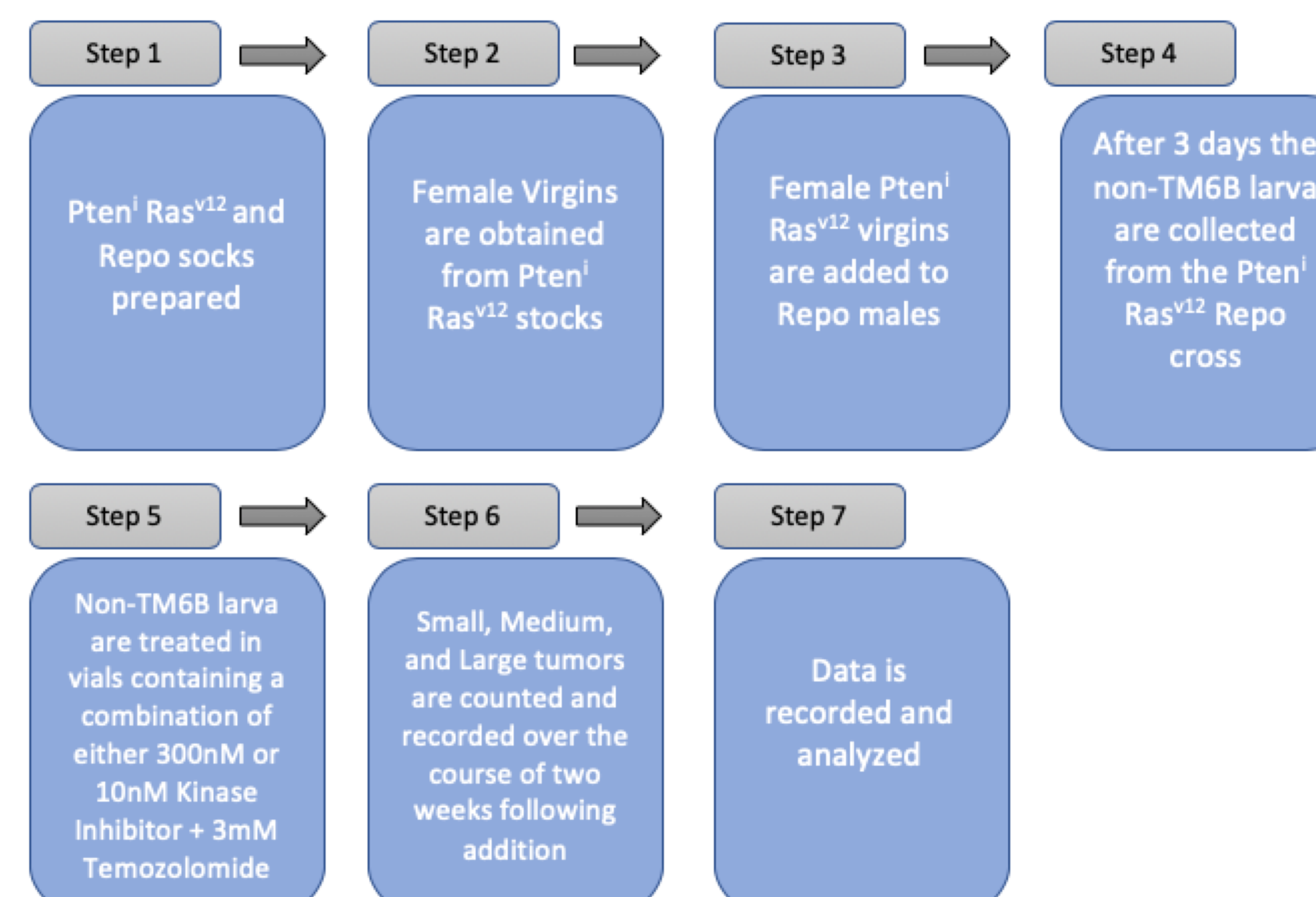
- Discovered that most effective concentration of Temozolomide was **3mM**



## Objectives

- Test combinatorial effects of each drug from the chemical screen with 3mM Temozolomide [a known effective concentration of Temozolomide]
- Test the drug combinations for dose range and target specificity. Find out if Temozolomide plus a given drug act via the target pathways or other downstream effectors.
- Our studies in *Drosophila* are expected to generate insights on possible modes of action of validated drugs.
- Validated drugs will be tested in mammalian models (by our collaborators) for their efficacy and specificity to identify the candidate-drugs for further studies in clinical trials in the future.

## Methodology



## Future Directions

- Continue chemical screen through Plate 1 (Drugs A-H).
- Test for combinatorial effects with Tyrosine Kinase Inhibitors determined in the Primary Drug Screen.
- Test the drug combinations for dose range and target specificity.
- Use Western Blotting to determine Mode of Action

## Acknowledgements

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